

REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 20-26 and 28-35 are pending in the present application. Claims 20-26 and 28-35 have been amended to more particularly point and distinctly claim the present invention. Claim 27 has been canceled.

In the outstanding Official Action, claims 20, 24, 30 and 35 were objected for allegedly containing grammatical errors. Applicants believe that the present amendment obviates this objection.

As suggested by the Examiner, the phrase "An oligomeric conjugate positively charged" will be deleted and the phrase "A positively charged oligomeric conjugate" will be inserted in claims 20 and 35.

As to claim 24, the applicant believes that the terms "imidazole" and "imidazol" are proper. "Imidazole" is recited when it is placed at the end of a chemical group denomination and "imidazol" is used when is placed in the middle of a chemical group denomination. As suggested by the Examiner, the term "metyl" and "limidazol" are replaced by their correct form.

As suggested by the Examiner, the "in" claim 30 has been deleted and the term "into" has been inserted.

Thus, in view of the above, applicant believes that the claims have been amended to overcome the objections. At this time, applicants would like to thank the Examiner for the suggestions as to how to overcome these objections.

Claims 20-25 were rejected under 35 USC 112, second paragraph for allegedly being indefinite. Applicant believes that the present amendment obviates this rejection.

As noted above, claims 20-35 have been amended to more particularly point out and distinctly claim the present invention. As to the term "substituted", in the context of NH_3^+ groups, the term corresponds to the substitution of one of the H atoms of the NH_3^+ group, in items a) and b), as well as in the item c) of claim 20. As described in the specification at page 9, lines 30-35 or page 12 lines 21, 27 or 34, the NH_3^+ group of each monomer may be substituted by one of three structures recited in a Markush group.

Regarding the claims rejected for reciting the term "monomeric component", the claims have been amended to recite that the "monomeric components" comprise monomeric components having substituted NH_3^+ and monomeric components having unsubstituted NH_3^+ . Monomeric components having substituted NH_3^+ represent at least 50% of the monomeric components.

As to the rejections of claims 20 and 35 for reciting the phrase, "protonable residues are not recognized as a recognition signal recognized by a cellular membrane receptor",

the claims have been amended to recite that the protonable residues may be chosen from imidazoles, quinolines, pterines, and pyridines.

As to the to the substituted position of the monomeric component, the substitution may take place on the free NH_3^+ of monomer by a protonable residue with a frequency of substitution of at least 50% of the monomers (page 3, lines 8-12); on the free NH_3^+ of monomer by an uncharged residue (page 3, lines 20-22); on the free NH_3^+ of monomer by a recognition signal (page 3, lines 23-24); on the uncharged residues placed on the NH_3^+ of monomer by a recognition signal (page 3, lines 27-28); on the protonable residue placed on the NH_3^+ of monomer by a recognition signal (page 3, lines 29-30) ;or on the NH_3^+ on the protonable residue placed on the NH_3^+ of monomer by a recognition signal (page 4, lines 1-3). Thus, applicants believe that the claimed substitution is definite to one skilled in the art.

As to claim 25, applicants believe that while the terminology is broad, it is definite. The "-" represents a minus sign to show the last monomer bound to the oligomer, in which the CO_2 function is free ($\text{O}=\text{C}-\text{O}-$).

The Applicant would also like to point out that the meaning of "R" is defined. A part of R (50 to 100 % of the polymerization degree, represented by the number "u") is chosen in the group consisting of the Markush group. In particular, the

Examiner's attention is directed to page 9, lines 29-40 and page 10, lines 1-6. When not 100%, R is chosen among this first group, the remainder of group R (represented by the "f" letter) may be chosen in the group consisting of the structure depicted at page 10, lines 29-32 to page 11, lines 16.

For example, when 70% of R is chosen among the Markush group, 30% are chosen in the second group of structure. Therefore, the number "f" is comprised between zero and the number "u" ($0 < f \leq u$), so between 0 to 50% of the polymerization degree.

In addition, a situation of less than 50% of R selected in the Markush group is not possible because of the general definition, wherein monomeric components having substituted NH_3^+ represent at least 50% of the monomeric components.

Regarding claim 25 and the dependent claims rejected because the equations involving the quantity "u", the number "u" represents the number of R substituted by a structure depicted in the Markush group. "u" is comprised between 50 and 100 % of the polymerization degree. The number "u" depends on the percentage of the residues R that are one of the structures mentioned above. It is necessarily an absolute number because "i", the degree of polymerization, is an absolute number. So, the upper limit of the number "u" cannot be superior to "i", the polymerization degree.

Thus, the expression $i = u + j + k + h$ is definite; u cannot be greater than i .

Claims 20-35 were rejected under 35 USC 112, first paragraph, for allegedly not satisfying the enablement requirement. Applicants believe that the present amendment obviates this rejection.

As noted above, claims 20-35 have been amended to further characterize the claimed oligomeric complex. As a result, applicants believe that this rejection has been obviated. Moreover, applicants note that claim 33 has been amended so the term "pharmaceutical" is no longer recited.

As a result, applicants believe that claims 20-35 are supported by the present disclosure.

Claims 20-26 and 35 were rejected under 35 USC 103(a) as allegedly being unpatentable over Midoux et al (WO 98/22610). This rejection is respectfully traversed.

The WO 98/22 610 publication is directed to DNA transfection whereas the present invention is appropriate for oligonucleotide transfection. As a result, applicant believes that the teaching of the WO 98/22 610 publication does not provide the motivation for one skilled in the art to modify its teachings to select a degree of polymerization and a percentage of substitution of oligomers as set forth in the present invention.

Indeed, a particular parameter or variable must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the parameter or variable might be characterized as routine or obvious. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). See also *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980). As the teaching of the WO 98/22 610 publication does not provide the motivation for one skilled in the art to modify its teachings to select a degree of polymerization and a percentage of substitution of oligomers as set forth in the present invention, applicants believe that the WO 98/22 610 publication fails to render obvious the claimed invention.

As a result, applicants request that the rejection be withdrawn.

Claims 20-26 and 33-35 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being obvious claims 1-6 and 10-15 of U.S. Patent 6,372,499. This rejection is respectfully traversed.

As noted in the Office Action, the WO 98/22610 publication was filed as PCT/FR97/02022 and is the priority document for U.S. Patent 6,372,499. However, as noted above, the teaching of the publications do not provide the motivation for one skilled in the art to modify its teachings to select a degree of polymerization and a percentage of substitution of oligomers as set forth in the present invention. As a result,

applicants believe that the double patenting rejection is improper and request that it be withdrawn.

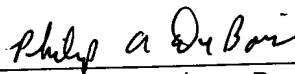
In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 20-26 and 28-35, as presented. Allowance and passage to issue on that basis are accordingly respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON


Philip A. DuBois, Reg. No. 50,696
745 South 23rd Street
Arlington, VA 22202
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

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